SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name: Endocapsular Ring

Device Trade Name: Capsular Tension Ring – Types 14, 14A and 14C

Applicant's Name and Address:
Morcher GmbH
Kapuzinerweg 12
D-70374 STUTTGART
Deutschland BR GERMANY

Applicant's U.S. Representative:
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U.S. Representative for Morcher GmbH
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Date of Panel Recommendation: January 17, 2002

Premarket Approval Application (PMA) Number: P010059

Date of Notice of Approval to Applicant: October 23, 2003

II. INDICATIONS FOR USE

For the stabilization of the crystalline lens capsule in the presence of weak or partially absent zonules in adult patients undergoing cataract extraction with intraocular lens implantation. Conditions associated with weak or partially absent zonules may include primary zonular weakness (e.g., Marfan's Syndrome), secondary zonular weakness (e.g., trauma or vitrectomy), cases of zonulysis, cases of pseudoexfoliation and cases of Marchesani's Syndrome.

III. CONTRAINDICATIONS

The Capsular Tension Ring should not be used in children 12 years of age or younger since this device is contraindicated in eyes still growing.

The MORCHER® Capsular Tension Ring is contraindicated for patients with perforated or damaged capsules.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Capsular Tension Ring labeling.

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V. DEVICE DESCRIPTION

The Capsular Tension Ring is a sterile, non-optical ocular implant that is permanently inserted into the crystalline lens capsular bag during intraocular lens surgery. The device acts to stabilize the capsule in the case of damaged or missing supporting zonules by circularly expanding the capsular bag. The Capsular Tension Ring is a circular ring, approximately 0.2 mm in cross-section, interrupted by positioning hole ends, and made of ultraviolet light(UV)-absorbing polymethylmethacrylate (PMMA). The three Capsular Tension Ring models (14, 14A, and 14C) differ primarily in their overall diameters (12.32, 14.5 and 13.0 mm, respectively), and compressed diameters (10, 12, and 11mm, respectively). Additionally, the Type 14A is a more-rigid design. The PMMA material is mdp 50 which contains 0.5% Tinuvin 326 UV-Absorber. The device is sterilized by gamma irradiation.

VI. ALTERNATIVE PRACTICES OR PROCEDURES

The conventional procedure used in the implantation of intraocular lenses in patients with damaged or weakened zonules involves suturing of the intraocular lens to prevent dislocation, or the use of an anterior chamber lens. There are no other PMA approved devices for treating weakened or damaged zonules.

VII. MARKETING HISTORY

The Capsular Tension Ring was first introduced outside of the United States in 1991. The Capsular Tension Ring has been marketed in 45 countries. The Capsular Tension Ring has not been withdrawn from marketing for any reason relating to the safety and effectiveness of the device.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Refer to Table 5 in the Summary of Clinical Studies below, and the labeling, for a summary of the adverse events and complications observed in the clinical study. Additionally, the potential adverse effects include the risks commonly associated with cataract removal and intraocular lens implantation.

IX. SUMMARY OF PRECLINICAL STUDIES

There is no performance standard or FDA guidance for this device. The applicant performed non-clinical studies on the device to establish a reasonable assurance of the safety and effectiveness of the Capsular Tension Ring from a non-clinical perspective (i.e., chemistry, engineering, microbiology, and limited toxicology).

Historical use of the material and similar materials (PMMAs) for intraocular devices, combined with the applicant's clinical study results and limited toxicology testing, were considered adequate justification for the omission of a complete battery of

biocompatibility tests, and established the suitability of the material.

The adequacy of the manufacturing processes, including sterilization, was established through review of manufacturing information and validations in the PMA as well as through on-site inspections. The non-clinical data provides a reasonable assurance of the safety and effectiveness of this device from chemistry, toxicology, engineering, microbiology and manufacturing perspectives.

X. SUMMARY OF CLINICAL STUDIES

Objectives

The objectives of the clinical studies were to assess the safety and effectiveness of the Capsular Tension Ring for stabilizing the crystalline lens capsule in patients with damaged or missing zonules undergoing cataract extraction with intraocular lens implantation.

Study Design

The study was conducted in two phases. Phase I consisted of 75 subjects and 11 investigators (5 sites), followed post-operatively for two years. Phase II opened the study to additional investigators for compassionate use of the device, and the subjects were followed post-operatively for a minimum of one year. Phase II also included subjects treated by the Phase I investigators beyond the initial 75 subjects.

The PMA subject cohort is the subjects treated by the Phase I investigators in both Phase I and II of the study, and represents 316 eyes of 268 subjects. Not including the subjects in Phase II that are part of the PMA cohort, the Phase II data represents 275 eyes of 253 subjects, and is considered confirmatory data.

Inclusion criteria for the clinical study were as follows: 18 years of age or older; cataract diagnosis and planned cataract removal with intraocular lens implantation; and diagnosis of pseudoexfoliation syndrome, Marfan's syndrome, zonular dehiscence due to trauma, suspected zonular injury, and/or prior vitrectomy following retinal detachment. There were no exclusion criteria.

The effectiveness endpoints for the study were intraocular lens centration and the degree of capsular fibrosis and contraction. The secondary effectiveness endpoint was visual acuity. Safety endpoints for the study were adverse events compared against the FDA's historical control for posterior chamber intraocular lenses reported in FDA's October 14, 1999 Draft Intraocular Lens Guidance Document.

Patient Assessments

Post-operative follow-up visits occurred at 1 day, 1 to 2 weeks, 3 months (10 to 14

weeks), 6 months (22 to 26 weeks), 1 year (11 to 13 months), and 2 years (23-25 months). Assessments included: pre-operative visual acuity, refraction, dilated fundus exam, zonular status (percentage of dehiscence and cause of dehiscence); intra-operative complications and percentage of zonular dehiscence; and post-operative haptic position relative to Capsular Tension Ring holes, amount of inflammation, and posterior capsule opacification/fibrosis.

Data Analysis and Results

The data summaries presented are for the PMA cohort (316 eyes of 268 subjects). The confirmatory data is addressed separately below.

Demographic Data

The population at risk for developing visually-disabling cataracts and needing cataract surgery is typically elderly; the elderly population has a slightly higher proportion of females to males. The PMA subject cohort was 51% females and 49% males. The inclusion/exclusion criteria did not exclude patients on the basis of gender or gender-related pathology. The average age of the subjects at the time of surgery was 68.6 years. The age range of the subjects was 26 to 94 years, with 73 <60 years, 49 from 60 to 69 years, 94 from 70 to 79 years, and 52 >79 years. The sponsor did not collect race or ethnicity data.

Accountability

The PMA cohort consists of subjects from Phase I and II, which had a study length of 2 years and 1 year, respectively. Therefore, the accountability analysis for the PMA cohort is separated by the phases. The study began on December 2, 1996 and the last PMA cohort subject was enrolled on May 16, 2001. The database cut-off date for the PMA cohort was October 1, 2001.

For the PMA cohort Phase I subjects, 49 (65.3%) of the enrolled subjects completed the study (2- year visit). Of the remaining 26 subjects, none remained active (i.e., not yet reached the 2-year visit); 4 were lost-to-follow-up; 3 died prior to completion of the 2-year visit; 5 withdrew, and 14 missed the 2-year visit. Sixty-four (85.3%) of the enrolled subjects completed the 1-year visit. Of the remaining 11 subjects at the 1-year visit, 8 were lost-to-follow-up; 1 died prior to completion of the 1-year visit, and 2 missed the 1-year visit, but were seen at a later visit.

For the PMA cohort Phase II subjects, 131 (67.9%) of the enrolled subjects completed the study (1-year visit). Of the remaining 62 subjects, 17 remained active (i.e., not yet reached the 1-year visit); 18 were lost-to-follow-up; 5 died prior to completion of the 1-year visit; 14 missed the 1-year visit, but were seen at a later visit; and 8 missed the 1-year visit.

Study Results

Table 1: Percentage of Zonular Dehiscence at Operation:

Amount of Zonular Dehiscence	*n/N (%)*
0%	109/316 (34.5%)
>0 to 25%	77/316 (24.4%)
>25% to 50%	29/316 (9.2%)
>50% to 75%	8/316 (2.5%)
>75% to 100% (360°)	5/316 (1.6%)
Unknown	88/316 (27.8%)
Total	316/316 eyes (100%)

- n = number of eyes with corresponding amount of zonular dehiscence, N = total number of eyes.

Table 2: Intraocular Lens Decentration at Last Available Visit:

Amount of Decentration (mm)	*n (%)*
No Decentration	297 (94%)
≤0.50	6 (1.9%)
0.51 to 1.0	5 (1.6%)
1.10 to 2.0	5 (1.6%)
Unknown	3 (0.9%)
Total	316/316 eyes (100%)

- Note, decentration rates may be higher, as it was not always reported whether the data was collected under dilated conditions or not.
- Nd:YAG treatment for posterior capsular opacities did not affect lens centration. Nd:YAG treatments were performed on 65 eyes (59 subjects).

Table 3: Last Corrected Visual Acuity at 10-14 Weeks or Later Stratified by Zonular Dehiscence at Surgery:

Percentage of Zonular Dehiscence	Corrected Visual Acuity	
	20/40 or better n/N (%)	Worse than 20/40 n/N (%)
0%	92/104 (88.5%)	12/104 (11.5%)
>0 to 25%	60/73 (82.2%)	13/73 (17.8%)
>25% to 50%	21/27 (77.8%)	6/27 (22.2%)
>50% to 75%	4/7 (57.1%)	3/7 (42.9%)
>75% to 100% (360°)	4/4 (100%)	NA
Unknown	72/83 (86.7%)	11/83 (13.3%)
Total	253/298 (84.9%)	45/294 (15.3%)

- n = number of eyes with corresponding visual acuity, N = total number of eyes with visual acuity reported.
- Eyes with uncorrected visual acuity ≥20/40, and no reported corrected visual acuity, were assumed to have a corrected visual acuity ≥20/40.

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- Visual acuity data was not available for 18 eyes.

For the study population, 224/316 (70.9%) of eyes had pre-existing pathology. Overall, 187/224 (83.5%) of eyes with pre-existing pathology achieved a corrected visual acuity of 20/40 or better, and 66/74 (89.2%) of eyes without pre-existing pathology achieved a corrected visual acuity of 20/40 or better.

Table 4: Last Corrected Visual Acuity at 10-14 Weeks or Later Stratified by Preoperative Pathology:

Preoperative Pathology	Corrected Visual Acuity	
	20/40 or better n/N (%)	Worse than 20/40 n/N (%)
Pseudoexfoliation	81/92 (88.0%)	11/92 (12.0%)
Glaucoma	40/49 (81.6%)	9/49 (18.4%)
Previous filtering surgery	11/12 (91.7%)	1/12 (8.3%)
Poor pupil dilation	18/21 (85.7%)	3/21 (14.3%)
History of uveitis	1/2 (50.0%)	1/2 (50.0%)
Previous retinal detachment	6/13 (46.2%)	7/13 (53.8%)
Diabetic retinopathy	3/6 (50.0%)	3/6 (50.0%)
Macular degeneration	17/31 (54.8%)	14/31 (45.2%)
Amblyopia	4/5 (80.0%)	1/5 (20.0%)
Other	109/136 (80.1%)	27/136 (19.9%)
With any preoperative pathology	187/224 (83.5%)	37/224 (16.5%)
Without preoperative pathology	66/74 (89.2%)	8/74(10.8%)

- n = number of eyes with corresponding visual acuity in the preoperative pathology category, N = total number of eyes with visual acuity reported in the preoperative pathology category.
- Eyes with uncorrected visual acuity ≥20/40, and no reported corrected visual acuity, were assumed to have a corrected visual acuity ≥20/40.

Table 5: Persistent and Cumulative Adverse Events and Complications Sorted by Persistent Incidence Rate:

Adverse Events and Complications	Persistent n/N (%)	Cumulative n/N (%)
Macular degeneration	25/284 (8.8%)	40/316 (12.7%)
Posterior capsular opacity	23/284 (8.1%)	41/316 (13.0%)
IOL decentered	20/284 (7.0%)	29/316 (9.2%)
Elevated IOP	14/284 (4.9%)	56/316 (17.7%)
Optic atrophy	6/284 (2.1%)	17/316 (5.4%)
Retinal detachment	6/284 (2.1%)	6/316 (1.9%)
Deposits on IOL	4/282 (1.4%)	12/316 (3.8%)
Iritis	3/284 (1.1%)	8/316 (2.5%)

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Cystoid macular edema	3/284 (1.1%)	7/316 (2.2%)
Posterior synechiae	2/284 (0.7%)	5/316 (1.6%)
Blepharitis	2/284 (0.7%)	3/316 (0.9%)
Retinal pigment epithelium	2/284 (0.7%)	2/316 (0.6%)
Glaucoma	1/284 (0.4%)	6/316 (1.9%)
Corneal Edema	1/284 (0.4%)	4/316 (1.3%)
Iridodonesis	1/284 (0.4%)	4/316 (1.3%)
Striae	1/284 (0.4%)	4/316 (1.3%)
AC inflammation	NA	147/316 (46.5%)
Cortical remnants	NA	8/316 (2.5%)
Vitreous problems	NA	8/316 (2.5%)
Drusen	NA	7/316 (2.2%)
Fibrin in pupil	NA	4/316 (1.3%)

- Persistent adverse events are defined as occurring at the 1-year visit or later, and represents 284 eyes of 241 subjects.
- Cumulative adverse events are defined as occurring at any visit, and represents 316 eyes of 268 subjects.
- AC Inflammation is tabulated for that occurring within the 1 day to 2 week post-operative period.
- Persistent and cumulative rates greater than 1% are reported.
- Adverse event and complication rates were not increased over that expected for cataract surgery.

Confirmatory Data

The confirmatory data represents subjects treated by investigators who may have only treated one or a small number of subjects under the compassionate use arm of the study. The applicant submitted, and FDA reviewed this data for consistency with the PMA cohort data. The safety and effectiveness data were substantially similar to the PMA cohort data.

XI. CONCLUSIONS DRAWN FROM THE STUDIES

The data in this application support a reasonable assurance of the safety and effectiveness of the Capsular Tension Ring when used in accordance with the indications for use and directions.

XII. PANEL RECOMMENDATION

At an advisory meeting held on January 17, 2002, the Ophthalmic Devices Panel recommended that Morcher's PMA for the Capsular Tension Ring be approved subject to submission to, and approval by, the Center for Devices and Radiological Health (CDRH) of the following:

1. The Indications for Use should be revised as follows:

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- For the stabilization of the crystalline lens capsule in the presence of weak or partially absent zonules in patients aged 18 years or older.

2. Provide line data on the following:
   - Adverse event complications of Core Phase I and Core Phase II patients, including glaucoma, uveitis, cystoid macular edema, retinal detachment, branch retinal vein occlusion, phthisis, broken eyelets, and device explantation.
   - Visual acuities of 20/40 or better preoperatively.
   - Visual acuities of worse than 20/40 postoperatively.
   - Information on the intraoperative estimate of amount ("clock hours") of intact zonules.
   - Evaluation of lens centration on postoperative dilated eye examination, including the percentage of cases already examined with dilation.

3. The labeling should be revised as follows:
   - Addition of a physician information booklet that should include:
     - The available ring sizes, with the justification for selection.
     - Data and information on the manual and "shooter" insertion and removal techniques.
     - Outcomes analysis of clinical study.
     - Possible indications for pseudoexfoliation, 1° zonular weakness (Marfan's Syndrome), 2° zonular weakness (trauma), and prior vitrectomy, as examples.
   - Line data summaries from #2 above.
   - A statement that the endocapsular ring does not alter the progression of zonular instability over time.
   - Specific information on the degree of zonular damage treated in the study.
   - Cautionary statement regarding the use of the device in an eye with large areas of zonular damage.
   - Remove the following contraindications from the labeling: during the first year of life, chronic uveitis, progressive eye disease (diabetic retinopathy, uncontrolled glaucoma), and operative complications in cataract operations (prolapse of the vitreous body, bleeding).

4. Provide a patient device implantation card for patient receiving the device.

XIII. CDRH DECISION

The Capsular Tension Ring was granted expedited review status on November 14, 2001 because there is no approved alternative device, and the device represented a specific public health benefit for which the alternative treatment would entail substantial risk of morbidity for the patient.

Following the panel meeting on January 17, 2002, FDA issued subsequent deficiency letters, and worked interactively with Morcher to resolve the remaining issues. FDA agreed with the Panel's recommendations. Morcher submitted responses that adequately

addressed all of FDA's concerns and labeling changes. The applicant's manufacturing facility was inspected on May 15, 2002 and was found to be in compliance with the Quality Systems Regulation (21 CFR 820). CDRH issued an approval order on October 23, 2003.

XIV. APPROVAL SPECIFICATIONS

Directions for use: See the labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions and Adverse Events in the labeling.

Postapproval Requirements and Restrictions: See approval order.

XV. REFERENCES

None.